THE MANAGEMENT OF THE ACUTE EPISODE IN CORONARY OCCLUSION*

CLARENCE E. DE LA CHAPELLE

Professor of Clinical Medicine, New York University College of Medicine

RECENTLY the United States Census Bureau[1] reported that the death rate from heart diseases has more than doubled during the last 40 years. Deaths from heart diseases in 1940 totaled 385,191, a rate of 292.5 per 100,000 population. This was the greatest number of deaths ever recorded from heart diseases.

Although there have been appreciable decreases in heart disease death rates in the low age brackets, the rate of heart disease fatalities has increased considerably in the upper age groups; for example, 45 to 54 years from 173.01 to 279.5; 55 to 64 years from 414.1 to 713.5; from 65 to 74 years from 957.3 to 1,723.5. Most of the deaths in these groups were due to coronary artery disease or its complications including coronary occlusion and myocardial infarction. This gives some idea of the prevalence of the condition, treatment of which I have been assigned to discuss this afternoon.

Definition of terms: The title of this discussion would probably be more correct if myocardial infarction were used in place of coronary occlusion. Recently some confusion has arisen concerning the terminology in coronary artery disease, due probably to several new expressions suggested such as coronary occlusion, coronary failure and coronary insufficiency. The term acute myocardial infarction seems to fulfill the requirements since the clinical signs and symptoms are all on the basis of myocardial necrosis. Then too, it is known that this lesion may occur without coronary thrombosis or without acute coronary occlusion, and contrariwise, occlusion or thrombosis of a coronary artery may occur without producing a myocardial infarct. As the studies of Blumgart and Schlesinger indicate, there is no characteristic clinical syndrome associated with coronary artery occlusion per se. The symptoma-

* Presented October 28, 1942 at The New York Academy of Medicine in the Refresher Lecture Course in Cardiovascular Diseases sponsored by The New York Academy of Medicine and the New York Heart Association.

tology is usually the result of an infarct.

Arbitrarily the first three weeks were chosen as the phase of myocardial infarction to be considered in this talk. An analysis of some 200 cases of myocardial infarction[2] on the Third (New York University) Medical Division of Bellevue Hospital demonstrated that most of the complications and sudden deaths occur during the three weeks after the onset of the illness. It is obvious, therefore, that this is the critical period of the disease.

Diagnosis: In the typical case of myocardial infarction the diagnosis is easy, in fact, is often apparent from the history alone. Although the problem of diagnosis will not be discussed, I should like to stress the importance of early recognition and the institution of immediate treatment since they have a decided influence on mortality as well as future expectancy of life. As already mentioned the early phase of this disease is usually the critical period. In a patient in whom a diagnosis is not obvious bedrest should be maintained until the correct diagnosis is decided upon and thereby give the patient the benefit of the doubt. The subsequent appearance of additional clinical manifestations indicative of infarction and the alterations in repeated electrocardiograms will usually establish the true nature of the disease even in the bizarre or atypical cases.

Treatment: Thrombosis which is the precipitating factor in some 60 per cent of cases with myocardial infarction is not instantaneous and may extend over a period of hours, days or weeks. Premonitory symptoms in such instances may precede the acute episode of infarction over the same period of time. It has been suggested that heparin, and more recently dicoumarin[3] (dicumarol), the new anticoagulant, might be useful in such cases in preventing complete obstruction and, in turn, infarction. Experimentally the basis for this rests in the work of Best and his collaborators[4,5] in dogs in whom heparin prevented the thrombosis which usually occurs in their coronary arteries after sodium ricinoleate has been injected into these vessels. This suggested the possibility of its use clinically in the initial stages of coronary thrombosis; or, if thrombosis be already complete, heparin might arrest its extension, or prevent mural thrombosis which not infrequently occurs in the ventricles over the site of the infarct and which acts as a source of emboli.

I have failed to find any reference in the literature relating to such use of heparin. Best[5] states that "it has been used in a few cases of coron-

ary thrombosis in human beings but not as yet in a scientific manner." Several isolated cases apparently have been known to have been reported at various meetings but these have not as yet been published.

As to dicoumarin (dicumarol) the new anticoagulant agent isolated from spoiled sweet clover, I have just been informed that it has been employed recently in four cases of coronary thrombosis, one under the supervision of Duryee[6] at the New York Post-Graduate Hospital and the other three at Welfare Hospital under Prandoni.[6] In all four instances it was administered in doses of 100 mgm. per day by mouth over periods ranging from twenty-one to twenty-eight days. All four patients had uneventful courses and recovered.

It is Best's[7] feeling, and I agree heartily with him, that the results in a few cases in which any anticoagulants have been employed are not significant, and that until a series of such cases with adequate controls have been made available, it is rather useless to discuss the results of the use of anticoagulants in the treatment of clinical coronary disease.

As soon as the diagnosis has been established every effort should be made to obtain complete physical and mental rest for the patient. He should be put to bed immediately, preferably in a Gatch bed, and not moved from it for at least a month. If transportation is necessary it should be by means of an ambulance and, if possible, postponed until at least the end of the third week. Under no circumstances should he be moved to a hospital merely to obtain special records such as electrocardiograms or other laboratory data.

The mainstay in the management of this disease is the reduction to a minimum of the demands on the heart and circulation. To this end the patient should be kept in bed and not be permitted to move about unnecessarily. During the first week or so he should not feed himself. Examinations of the patient, with the exception of auscultation of the anterior chest, should be infrequent during the first few days.

Special nursing care should be instituted immediately. Day and night nurses are essential with special attention to the ability of the night nurse who should be alert and conscientious during her stay on duty. Careful nursing is one of the most important factors in the successful recovery of the patient. No visitors except those in the immediate family should be allowed in the sick-room during the first week. All visits should be curtailed to only a few minutes.

Complete mental relaxation bordering on drowsiness should be maintained during the first few days or even the first week. Highly excitable, apprehensive or temperamental patients are much better off if kept asleep more or less continuously during the early phase of the illness. Some form of a sedative or an opiate may be required to accomplish this. In the absence of pain one of the barbituric acid preparations such as phenobarbital in doses of 30 mgm. (½ gr.) or amytal 0.1 gm. (1½ gr.) given three times a day may be sufficient to keep the patient at ease, drowsy or even asleep. Chloral hydrate or sodium bromide or both may also be given several times daily with good results.

Before leaving this part of the treatment, let me remind you that alcohol is of distinct benefit in the therapy of myocardial infarction. It induces in most individuals peripheral and possibly coronary vasodilatation. Incidentally, Heberden demonstrated long ago that alcohol might not only abort but even prevent angina pectoris in many instances if employed in timely doses. In many patients alcohol produces tranquility and relaxation as well as creating a sense of well-being. To obtain the maximum good effect from its use, alcohol should be administered in that form agreeable to the patient. This is often decided by individual taste or preference although occasionally by race and custom. Consider the likes and dislikes of the patient, and do not give it to those who dislike it in any form. Needless to say do not continue to use it when it fails to be of benefit. Discontinue it if the patient becomes depressed under its influence or if it causes gastric hyperacidity or heart-burn. More often, however, some form of alcohol offsets the depression incident to myocardial infarction and its prolonged period of bedrest and disability.

Small doses such as 15 to 30 cc. (½ to 1 oz.) repeated two or three times a day are preferable to larger amounts given once a day. Let me also stress the importance of not giving alcoholic beverages with large amounts of iced, charged water. Whiskey can be given with plain tap water or small amounts of a natural effervescent water; rum in hot, weak tea is excellent and brandy or sherry may be taken straight or in a frappé. Another pleasant drink and food is bourbon whiskey served in an egg-nog made with milk instead of cream. One of the most pleasant effects of alcohol is its sedative and hypnotic action. A glass of wine, sherry or beer, or a "hot toddy" will often prepare the patient for sound sleep. This will negate the need for drug administration and may result

in a night of normal sleep.

Coffee should be prohibited at least during the first week and preferably for the entire illness. It does no good, despite the fact that caffeine is supposed to cause coronary dilatation;[8] causes precordial pain; and not infrequently does harm by increasing the nervous tension of the patient or instigating the production of premature systoles.

Tobacco of any type should be stopped as soon as the diagnosis of myocardial infarction has been made and the patient should discontinue smoking for at least the remainder of the illness. It is harmful and may actually induce attacks of angina in a goodly proportion of patients with this disease. What the underlying mechanism in the heart may be cannot be definitely stated but, judging by the recent report of Wilson and Johnston,[9] it is quite likely to be one of vasoconstriction of the coronary arteries. It would seem, therefore, to be a wise policy to curtail its use at least during the period of bed confinement, although it would also seem the part of wisdom for anyone who has suffered a coronary occlusion to abstain permanently from it.

Diet: A low calorie diet is essential in decreasing the metabolic rate and in turn reducing the demands on the heart. It also prevents the patient from gaining excessive weight during the long period of bed confinement. If the patient is obese the use of a low calorie diet is definitely indicated since the greater the weight, the greater is the work load of the heart.

The diet should be liquid during the first few days with milk or milk with vichy, and warm broths, as the main constituents. These should be given approximately every three hours. Water should also be administered but total fluid intake should not exceed 1500 cc. in 24 hours, particularly if there are any suspicious signs of a failing heart. The Karell diet (200 cc. of milk given every four hours) is often employed during the first few days. Many patients are unable to tolerate the iced fruit juices that are so often given during the early phase of this illness. In fact iced drinks in general had better be avoided. Junket, custard, warm cooked cereal and some of the stewed fruits such as apple sauce and puréed vegetables may be added toward the end of the first week. If the patient is unable to take fluids or nourishment by mouth, particularly if vomiting is present, 50 cc. of 25 per cent glucose solution may be given intravenously twice daily together with 5 to 10 per cent glucose solution by rectum through a Harris drip. Large volumes of fluid,

especially infusions, are contraindicated because of the danger of pulmonary edema. If actual dehydration is present hypodermoclysis may be employed or rectal instillations may be given by catheter or Harris drip, usually 5 to 10 per cent solution of glucose in saline.

During the second and third weeks a more complete diet may gradually be resumed to include some solid foods such as chicken, fish, lamb chops, cooked vegetables without too much roughage, or which do not provoke flatulence, and some of the raw but readily digested fruits. An adequate supply of vitamins should be provided especially during the first week when food intake is restricted. Deficiency of Vitamin B_1 can lead to heart failure or aggravate the degree of failure which may be instigated by the myocardial infarct.

Bowel hygiene: Regulation of bowel function is essential but may be neglected, as a rule, during the first two or three days, particularly if food intake has been limited to fluids. Straining at defecation should be avoided by keeping the stool soft. This may be accomplished by giving sufficient fluids by mouth and the regular administration of 30 to 45 cc. (1 to 1½ oz.) of mineral oil every night followed in the morning by a small enema of oil and glycerine or saline. After the second or third day enemas may be given daily or every second day, if needed, for the next week or so. Subsequently mild catharsis may be stimulated by the use of milk of magnesia or any other mild laxative.

Abdominal distention is sometimes a problem in the early stage of myocardial infarction. Heat applied to the abdomen may give some relief, also the insertion of a small rectal tube. If not successful small turpentine enemas given with care may be employed. Pitressin[10] may be given but with caution since it is a coronary vasoconstrictor. The newer synthetic forms of atropine such as Novatropine or Trasentin are sometimes effective, particularly if distention is secondary to a spastic colon or some other neurogenic state. Small doses of fluid cascara given repeatedly will sometimes relieve distention.

Some modification in bowel hygiene may have to be made after the first week or so for those patients, usually men, who struggle with the bed-pan. A compromise may be made by allowing the use of a commode placed immediately adjacent to the bed onto which the patient may be lifted or slid by means of a special draw-sheet. Needless to say it is to be used only for bowel evacuation.

Management of immediate attack: Control of the severe substernal

pain or distress which introduces most of the attacks of myocardial infarction is highly essential. Nitrites are ineffective. In fact they may do harm and therefore should not be employed. They are especially dangerous if the patient is in shock. Morphine sulphate given subcutaneously in doses of 15 mgm. (¼ gr.) and repeated several times in the space of an hour or two if needed should be administered. Occasionally it fails to provide relief. Although it appears to be the drug of choice in quieting the patient and relieving pain during the period of severe distress and anxiety, it might be well not to repeat it too often since it not infrequently causes vomiting. If the patient is known to be sensitive to this drug Pantopon 20 mgm. (1/3 gr.) or Dilaudid 4 mgm. (1/12 gr.) may be used hypodermatically.

It may be appropriate here to mention the newer synthetic morphine substitutes which are at present only available for investigation purposes but which will probably be released to the profession in the near future. One of the most promising is known as "Metopon"[11] which is a methyl derivative of dilaudid. Its advantages over morphine include less respiratory depression, greater analgesic potency, less liability for producing addiction, and less noticeable emetic properties. Another one is "Demoral" which has recently been investigated clinically at Bellevue Hospital by Batterman.[12] It is a synthetic analgesic approaching the potency of morphine for the relief of pain. Although having a shorter duration of action, it has the advantage over the opiates in not resulting in respiratory or profound cerebral depression. Prolonged use with therapeutic doses has not resulted in primary addiction. Both these new drugs may some day be very useful adjuncts or may even replace the present day narcotics in the treatment of myocardial infarction.

Recently another drug has been advocated during the early phase of myocardial infarction. I refer to atropine sulphate which is supposed to counteract the efferent vagus action which induces reflex constriction in coronary vessels at the onset of attacks of coronary thrombosis. Experimental studies[13,14] suggest that this action of the vagus may aggravate the cardiac lesion already present and may even precipitate sudden death, probably by initiating ventricular fibrillation. Hence the use of atropine given intravenously in doses of 0.8 mgm. (1/75 gr.) which may be repeated several times daily during the acute stage particularly if pain continues. In the presence of a tachycardia, however, it should be withheld or given in distinctly smaller doses.

The experiments of Manning, McEachern and Hall[14,15] demonstrated that the ligation of a coronary artery of the dog causes a reflex vasoconstriction of the other coronary vessels. When a coronary artery was ligated under complete anesthesia, there was a low mortality, but if the ligatures were not tied until recovery from anesthesia, there was a high mortality. However, if the vagi were cut or atropine administered before the artery was ligated in the unanesthetized dog, the mortality remained at the same low level as when the artery was tied in the animal in whom the reflexes were abolished by complete anesthesia.

A year ago, during the Graduate Fortnight, Gilbert[16] in discussing "the influence of extrinsic factors on the coronary flow and clinical course of heart disease," referred to some unpublished work, subsequently reported,[13] which showed that the administration of a purine-base vasodilator, such as aminophylline, in addition to atropine, caused an even lower mortality when the coronary artery of a dog is ligated. They have already made use of these observations in the management of coronary occlusion in humans. By the immediate administration of atropine and aminophylline they believe that they have not only greatly reduced their mortality in early cases of coronary thrombosis but the recovery of their patients has been more rapid and more uneventful than previously.

Some authorities[17,18] use aminophylline alone, others[16] combine it with atropine or papaverine but both administer it intravenously in doses ranging from 0.24 to 0.48 gm. two to three times a day during the acute or critical phase of myocardial infarction. Both groups feel that the results obtained with aminophylline are due to an improvement of the collateral coronary circulation. My own experience with the intravenous use of aminophylline in myocardial infarction, either given alone or with atropine or papaverine, has been rather limited. I have seen satisfactory results in some cases, equivocal or even poor results in others. Although I believe these drugs are valuable in the treatment of an acute myocardial infarct I feel that administration intravenously should be restricted to the critically ill patients rather than given routinely.

If not obtainable in the 10 or 20 cc. ampule, aminophylline should be diluted to this amount with physiological saline, dextrose solution, or distilled water. Injection should be very slow and preferably through a fine gauge needle (22 gauge). Rapid injection may cause fulness in the

head or a throbbing headache, vertigo, palpitation, and even precordial pain or oppression. Occasional fainting may take place, especially in sensitive or neurotic patients.[18,19] Smaller doses such as 0.24 gm. (3¾ gr.) should be used in those patients with accelerated heart rates or whose blood pressure is very low, since the drug sometimes causes a fall in blood pressure and/or a tachycardia.

In some patients complete relief of substernal pain or distress is noted almost immediately, even in the absence of an opiate. Reduction in the amount of opiates administered is often possible. It sometimes may be withheld completely when aminophylline or atropine or papaverine are used. However, the latter drugs should not be employed to the exclusion of other important therapeutic measures and should be used with caution and discontinued with the appearance of severe reactions.

Aminophylline may also be given by mouth, preferably in the form of an enteric-coated capsule or tablet to avoid or reduce the gastric irritation which so frequently occurs in those individuals sensitive to the drug or in those patients in whom large doses have been employed. These symptoms include nausea or vomiting, burning epigastric pain, and distention. It may be given orally in doses of 0.2 gm. (3 gr.) three or four times a day for variable periods of time during the first month or two after the onset of the illness and subsequent to the intravenous use of the drug during the critical phase. Gastric irritation may be avoided by discontinuing the drug three to four days at a time, and then resuming for a week or ten days.

There is still considerable difference of opinion concerning the value of aminophylline as a coronary vasodilator both in animals and in man, and especially in the presence of coronary sclerosis or occlusion. Experimental studies in animals[20,21,22] have given variable, even contradictory, results. In man, however, Levy, et al.,[23] using induced anoxemia in individuals subject to attacks of angina caused by coronary sclerosis, found that aminophylline caused a prolongation of 63 per cent in the time of appearance of pain when given intravenously but only 26 per cent when taken by mouth. Clinical tests[24,25] controlled by placebos have shown that aminophylline or other xanthines administered orally have no superiority over the placebos. Others have[26,27] obtained good results with these drugs but employing considerably larger doses. Although the drug is not dangerous when given orally, its intravenous administration is known to have resulted in many instances of reactions, previously men-

tioned, which may be rather disturbing.[18] A few fatalities have been noted but not reported as far as I am able to ascertain. One observer[28] believes that he induced an attack of coronary occlusion in two patients with bronchial asthma—one associated with a previous myocardial infarct, the other probably with coronary sclerosis—by using 0.48 gm. of aminophylline intravenously. One of these patients succumbed three months later but no autopsy was obtained.

Fortunately, an appreciable number of patients follow a rather benign course from the onset of their myocardial infarct through to convalescence. Herrick referred briefly to these cases in his first communication in 1912. In these patients the pain not infrequently disappears shortly after onset or even before the physician's arrival and no other severe manifestations of the disease such as shock, embolization, or heart failure make their appearance. Needless to say, in such instances therapeutic measures can be quite limited and intravenous aminophylline or atropine or both are probably of doubtful value or even contraindicated. Overtreatment of the patient in such instances is more to be feared than neglect.

Papaverine: Although not a new preparation, this drug has had somewhat of a renascence, so to speak, in the past few years in the treatment of all forms of vascular disease. It is an opium alkaloid of low toxicity and non-habit forming. It has been shown to be very useful in coronary occlusion, chiefly because it is a powerful coronary vasodilator.[29] Experiments on dogs by McEachern and his Toronto group[30] show that the administration of this drug reduces the mortality resulting from ligation of a major coronary artery. Likewise, the experimental demonstration by Katz, et al.[31 32] that this agent reduces or abolishes induced premature contractions and decreases the ease with which ventricular fibrillation is induced in the dog, suggests the possibility of its clinical value in the treatment of premature systoles, and its use in conditions which are apt to lead to ventricular fibrillation.

As to its mode of action it has been credited by Katz[32] with the following effects: A mild sedative action, a definite and lasting coronary dilating action, and the prevention or lessening of the occurrence of premature systoles (auricular, nodal and ventricular) or certain types of rapid heart action like ventricular fibrillation. In this last respect it acts like, but apparently is superior to, quinidine, since it also has a coronary dilating action which quinidine lacks. Furthermore, it is not a

myocardial depressant like the latter drug.

Papaverine, therefore, may be of considerable value in fresh myocardial infarction since premature systoles occurring in this process represent an added burden on the heart and may, if of ventricular origin, result in ventricular tachycardia or fibrillation. Relief of pain in this disease has also been obtained by its intravenous use, employing it in doses of 60 to 90 mgm. (1 to 1½ gr.), repeated every two to three hours if necessary. Oral administration can be used to continue its desired effect, the usual dose then being 0.2 gm. (3 gr.) every three to four hours.

Oxygen therapy: In acute coronary occlusion a sudden interference with the flow of blood results in a severe oxygen-want in the myocardium. The use of oxygen in this disease was first suggested in 1929. In the following year and again in 1934 Levy and Barach[33] demonstrated its value as a therapeutic agent in this disease. According to these authorities[34] the basis of its use is founded on three facts: (1) "Anoxemia of the heart muscle occurs after sudden occlusion of a sizeable branch; (2) oxygen-want induces impairment of cardiac and respiratory activity; (3) the inhalation of oxygen in high concentration increases the oxygen content of the arterial blood and results in improvement in the functional capacity of the heart."

Oxygen administration in high concentration,[35] even in 100 per cent concentration for periods of approximately 12 hours, is particularly indicated in the patient with myocardial infarction who presents circulatory collapse, or severe pain and restlessness which does not respond to the opiates or other medications, and when there are evidences of a failing myocardium. The latter may be suggested by the appearance of cyanosis, tachycardia, gallop rhythm, low blood pressure, dyspnea, and signs of pulmonary congestion. It is also very effective in the treatment of pulmonary edema as a result of left ventricular failure, particularly if given by the positive pressure technique.[36] Paroxysmal dyspnea and Cheyne-Stokes breathing also respond to oxygen therapy.

Oxygen tents are capable of delivering and maintaining from 50 to 75 per cent of oxygen. They are comfortable to most patients. The oronasal catheter is simple and efficient but must be carefully placed under direct throat vision. It is said to deliver from 35 to 50 per cent of oxygen. Recently various types of masks have made their appearance including the well-known Boothby mask, both nasal and oronasal types,

which are capable of delivering up to 100 per cent oxygen. They are quite simple, efficient, inexpensive and easily adjusted. However, many patients complain that they are uncomfortable, especially in warm weather. Small face tents are also obtainable, made of transparent plastocele, which fit over the bridge of the nose and may easily be molded to the conformation of the patient's face. This may give oxygen concentration between 40 and 60 per cent. Many patients find this type more comfortable, especially in warm weather than the heavier rubber masks or the nasal catheters.

Complications: More than 50 per cent of the attacks of myocardial infarction are associated with complications and the majority of these occur during the first three weeks. A fairly common one is that of peripheral circulatory failure of some degree which invariably occurs with or immediately after the onset of the attack.

Acute circulatory failure or shock occurs in as high as 1/3 of cases as a complication of the immediate attack. It may introduce the picture in some instances, with pain as a minor symptom or entirely absent, but more often appears simultaneously with the pain. In other instances it occurs hours or days after the onset of pain. Its manifestations usually constitute a classical picture with cold clammy skin, rapid and shallow respirations with frequent sighing, gray, cyanotic pallor of the face which may be drawn and anxious, rapid, feeble pulse and depressed arterial pressure with small pulse pressure. Although a subnormal mouth temperature may be obtained, the rectal temperature is frequently elevated. The cause of this primary form of shock in coronary occlusion remains obscure. Some form of nervous mechanism seems a likely probability. Acute cardiac weakness and failure of the central driving force are undoubtedly contributing factors in the mechanism. A definite decrease in circulating blood volume has been demonstrated.[37] This may be the result of stasis in the vascular bed and an increase in capillary permeability secondary to tissue anoxia, and in turn resultant loss of plasma and other blood elements.

If the severe substernal pain which introduces the attack of myocardial infarction is not present during shock, morphine should not be administered unless anxiety and restlessness are prominent because it depresses pulmonary as well as tissue respiration and thereby aggravates the general anoxic state already present. High concentration of oxygen, 75 to 100 per cent, administered by one of the special face

masks or by tent should be instituted. Theoretically, vasoconstrictor drugs such as epinephrine should be of some benefit in the shock of myocardial infarction. However, only in rare instances do they seem to be of help. They should be used with caution and preferably in small doses such as 0.5 mgm. subcutaneously or intramuscularly, or 0.1 to 0.2 mgm. of a 1:1000 solution intravenously. Occasionally it is employed much diluted in an intravenous saline drip. It is well known that epinephrine administered to patients with coronary sclerosis readily initiates the anginal syndrome. Hence the caution with which it should be used for shock in coronary occlusion.

I have seen patients with myocardial infarction in shock respond to transfusions of blood or plasma. Such transfusions should be given in quantities ranging from 150 to 250 cc. They probably help by augmenting the decreased circulating blood volume. However, such transfusions should be given slowly in order to prevent overloading the already injured heart. Hypertonic glucose solutions by intravenous infusion may be given slowly in amounts of 100 cc. of a 50 per cent solution and repeated if needed. This may not only increase the circulating volume but also act as nourishment for the heart muscle. It also tends to increase venous return from the extremities to the heart. The intravenous administration of fluids may be hazardous and therefore should be employed with caution. The presence of any degree of heart failure, as determined by clinical or laboratory means (increased venous pressure), is an absolute contraindication.

Elevation of the foot of the bed should be done immediately. The patient should be covered with blankets but artificial heating methods should be withheld since recently some question as to the benefit of artificial heat has been raised. Burns may readily result because the constricted peripheral vessels cannot carry off the excess heat. Then too, if vasodilatation should occur, the blood pressure level will drop further. In addition, excessive sweating may cause further loss of body fluid. Bandaging the lower extremities from ankles to mid-thigh may also be of value. It has been shown that the circulating blood volume may be increased 1000 cc. by this procedure.[38]

Arrhythmias: Various forms of arrhythmias make up the second commonest complication in myocardial infarction. Some, such as complete heart block and ventricular tachycardia, are quite rare; others, such as premature systoles and paroxysmal auricular fibrillation, are more

common. Probably, most sudden deaths which occur during or after the immediate attack or in the first three weeks are due to ventricular fibrillation. Rupture of the heart is a much less frequent cause of sudden death.

Premature systoles, particularly of ventricular origin, are quite common during the early stage. Those occurring infrequently may be ignored unless annoying to the patient. They can usually be abolished by the use of quinidine in doses of 0.2 gm. (3gr.) three times a day or papaverine 0.2 gm. (3 gr.) every four hours. Either one of these drugs should definitely be used if the premature systoles occur frequently, i.e., once in every ten beats or in series, which suggests that they may be the forerunner of ventricular tachycardia. The latter rhythm has been shown to be the link which connects ventricular premature systoles with ventricular fibrillation.[39]

I see no justification in the routine administration of quinidine, as has been advocated, during the first two weeks as a prophylactic against the development of ventricular tachycardia or fibrillation. Both disturbances are quite uncommon in patients who survive the first 24 hours, which the majority do. Their onset is commonly preceded by frequent ventricular premature systoles which act as a warning and thereby permit the institution of corrective measures. Ventricular tachycardia is usually amenable to treatment. Also the efficiency of this measure has never been proven and seems rather difficult of proof. Lastly, since quinidine is a distinct myocardial depressant it seems best to employ it only when actually needed.

Ventricular tachycardia is always of serious significance since it may precipitate heart failure, embolism, ventricular fibrillation and sudden death. Although its recognition is only certain by means of the electrocardiogram, its presence should be suspected in any patient with myocardial infarction who suddenly exhibits a rapid rate ranging from 180 to 200 per minute which is basically regular in rhythm. Fortunately, the paroxysm may end spontaneously within a short period after onset. Others, however, continue for hours or even days.

Several drugs are known to influence this rhythm. They include quinidine salts, magnesium sulphate, and potassium chloride or acetate. When quinidine is to be administered, it is well to give a preliminary test dose of 0.2 gm. (3 gr.) by mouth and wait 30 minutes or so to note if any signs of sensitivity to the drug such as marked tinnitus, diarrhea

or vertigo appear. If not, then doses of 0.4 gm. or even 1 gm. (6 to 15 gr.) may be given at intervals of two or three hours until the bout terminates or signs of toxicity appear. Following return to normal, quinidine in doses of 0.2 gm. (3 gr.) three times daily after meals should be continued for the next week or two to diminish the possibility of recurrence.

Magnesium sulphate may be given intravenously in a 10 to 20 per cent solution in amounts up to 15 cc. It should be injected very slowly, pausing after every 5 cc. to check the heart rate since the attack may stop before the entire amount is injected. It acts by depressing the ectopic focus which is usually the infarct or muscle immediately adjacent to it.

Potassium salts are known to depress the conductivity and excitability of the myocardium. They are also known to potentiate digitalis and quinidine, and finally, when given alone, may abolish premature systoles and paroxysmal ventricular tachycardia.[40] Either potassium chloride or acetate[41] may be employed, using 1 to 2 gm. (15 to 30 gr.) every two to four hours by mouth, until a favorable response is obtained or a maximum of 10 gm. (150 gr.) has been administered.

Another procedure which may be tried, particularly if quinidine or the potassium salts alone are ineffective, is the administration of both drugs.[40] Quinidine is then given in full doses until 2 to 3 gm. (30 to 45 gr.) have been administered, at which time the potassium salts should be started.

Formerly quinine dihydrochloride was used intravenously to abolish prolonged attacks of ventricular tachycardia and more recently quinidine sulphate. However, the intravenous use of either drug is dangerous because of their severe reaction on the myocardium. Sudden death may occur with both and several such incidents have been reported. Only when all other measures have failed and the outlook appears hopeless would I suggest the intravenous administration of these drugs.

Paroxysmal auricular fibrillation occurred in 12 per cent of an unpublished series[2] of 200 cases with myocardial infarction at Bellevue Hospital. The majority of attacks are of short duration ending spontaneously. Some, however, continue for days or the rhythm may become established. It is the longer episodes which, as a rule, need treatment since they may, and not infrequently do, precipitate heart failure. The drug of choice in such instances is digitalis given in divided

doses and always by mouth. An initial dose of 0.4 gm. (6 gr.) may be given followed by 0.4 gm. (6 gr.) at intervals of six hours until normal rhythm returns or the ventricular rate reaches 70 or 80 per minute. If sinus rhythm is not obtained by digitalis, quinidine in doses of 0.3 gm. (5 gr.) at intervals of two hours may be employed. If not successful alone quinidine may be supplemented with strychnine sulphate 1.5 mgm. (1/40 gr.) three times a day. This combination has been shown by Smith and Boland[42] of the Mayo Clinic to be more efficacious in auricular fibrillation than when quinidine is administered alone and smaller doses of quinidine are required if strychnine is also administered. Should fibrillation persist despite quinidine therapy, digitalis may be resumed in maintenance doses of 0.1 gm. or 0.2 gm. once daily.

Congestive heart failure in our experience rarely occurs to any obvious degree in individuals sustaining their first attack of myocardial infarction unless they are 60 years or over, or have a complicating disease such as diabetes mellitus or hypertension.

The clinical signs of congestive failure may not be too obvious as judged by the usual manifestations of dyspnea, pulmonary rales, edema and engorged liver. Venous pressure determinations, however, are frequently elevated even in the absence of symptoms or when only a few basal rales may be the only indication of a failing heart.

The hypertensive cardiac who sustains a myocardial infarct, in contrast to the uncomplicated arteriosclerotic cardiac, quite often develops paroxysmal dyspnea as the prominent clinical phenomenon of acute left ventricular failure. Several therapeutic measures seem effective in this condition. First of all, morphine hypodermatically in a .15 mgm. (¼ gr.) dose should be given immediately. If available, administration of high concentration of oxygen by tent or mask is of value, and if pulmonary edema complicates the picture, it may be given under positive pressure.[36]

Venesection or phlebotomy may successfully be carried out by the removal of 500 cc. of blood. However, an effect similar to this may be obtained by applying blood pressure cuffs to the extremities and inflating them to a pressure slightly greater than the patient's diastolic pressure. Dramatic relief may be obtained by this means. The purpose is to utilize the peripheral venous system as a reservoir and thereby decrease the circulating blood volume. It has one drawback, it causes venous dilatation and thus may favor venous thrombosis and possibly emboli.

An instrument has recently been devised by Kountz et al.[43] which inflates and deflates cuffs, placed on the arms and thighs, in rotation. They believe that as much as an eighth of the total circulating blood volume may be impounded by their method of intermittent constriction. Their application of this procedure in patients with acute left ventricular failure usually resulted in dramatic improvement. They also suggest that acute myocardial infarction is another condition in which reduction of the quantity of blood-flow to the heart might be beneficial in minimizing the demands on the myocardium. In 10 patients with acute myocardial infarction this treatment was given for a period of 14 days. All of them survived, whereas the mortality rate of such patients in a hospital from which a similar group of patients was chosen, was 37 per cent. They state that although a more detailed study must be made before definite conclusions can be drawn, the results suggest that this treatment affords some protection to the heart when the function of the left ventricle is impaired.

Aminophylline, given intravenously in doses of 0.48 gm. (7½ gr.) in 10 or 20 cc. of saline or hypertonic glucose solution, is another drug which is quite effective in acute left ventricular failure. Concentrated glucose solution, such as 50 cc. of a 50 per cent solution, has also been employed alone, particularly when pulmonary edema is present, with seemingly good results.

Mercurial diuretics are of distinct value in acute failure although their full therapeutic action is delayed longer than the preparations and procedures just mentioned. However, because of the recent "wave" of reports in the medical literature[44,45] of instances of sudden death or severe reaction following their administration, it might be well to stress a few notes of caution:

1. Never use more than 2 cc. for the initial intravenous dose. A preliminary dose of 1 cc. intravenously would be preferable for the patient with myocardial infarction.

2. Always draw blood into the syringe before injecting the drug and take plenty of time to inject, employing a small calibre needle (25 gauge).

3. Check the patient for evidence of salt depletion. If present give sodium chloride for one or two days prior to the administration of the diuretic.

4. If the patient has been taking digitalis, be certain that the digitalis

dosage is well below the toxic level, or discontinue it for a day or two. It might be well also to use a small dose, i.e., 0.5 cc. to 1 cc., at the initial injection intravenously. Larger doses can be given later if satisfactory diuresis does not result.

Mercurial diuretics may be used rectally in suppository form; more recently a tablet has been offered for oral use. Neither one is as effective as the intravenous or intramuscular preparations. All forms of mercurial diuretics are made more effective by the administration by mouth of ammonium chloride, ammonium nitrate or potassium chloride, preferably given in enteric-coated capsules.

Although it is of distinct importance to call attention to the dangers of these diuretics it seems just as important not to exaggerate these dangers since these preparations constitute one of the most valuable groups of therapeutic agents in the treatment of diseases of the heart. As DeGraff[46] has stated, one must remember that the toxic reactions and deaths reported from mercurial diuretics are in reality only a very small number in relation to the extensive use of these drugs. These reports, therefore, should not discourage the rational use of these diuretics.[47]

Digitalis. I have purposely left this drug to the last because of its disputed status in myocardial infarction. As a rule digitalis is not needed in the immediate treatment of paroxysmal dyspnea with or without edema since the therapy just outlined is usually effective. However, since this mechanism is indicative of left ventricular failure it may be desirable in some instances to follow the administration of the rapidly acting drugs by digitalis with the hope of maintaining the patient's cardiac reserve.

Indications for the use of digitalis in myocardial infarction include (1) the appearance of progressive congestive failure, either with or without preceding left ventricular failure, which has not responded to the administration of mercurial diuretics, fluid intake restrictions, sedation, or high concentration of oxygen, and (2) the control of paroxysmal auricular fibrillation, particularly the attack with a rapid ventricular rate or that which is complicated by signs of congestive failure.

I would suggest that digitalis should always be given in such cases by mouth or by rectum and never intravenously. Dosage should be smaller than in the average cardiac and given more cautiously with care-

ful supervision during administration and frequent check-up for early therapeutic effect or toxic signs or symptoms. I would advise the general practitioner to use the tablet of U.S.P. powdered digitalis leaf in the patient with myocardial infarction rather than any of the new digitalis glycosides, at least for the present. Goodman[11] of New Haven pointed out in a recent lecture at the Academy that in the overwhelming majority of patients with heart failure one will find this preparation easy to administer, readily absorbed when given by mouth, effective in its action on the myocardium; also that it possesses an adequate amount of safety, is stable in potency, and cumulation and elimination occur in the body at rates allowing complete digitalization at varying speeds and satisfactory maintenance of desired therapeutic effects for long periods of time. Undoubtedly Doctor Gold will discuss this problem in detail in a subsequent lecture.

The fear of cardiac rupture in myocardial infarction due to digitalis therapy has been highly exaggerated. It may interest you to know that in a large series of myocardial infarcts with rupture reported from the Pathological Laboratory of Bellevue Hospital,[48] none of the individuals had received digitalis.

The other fear has more to substantiate it, namely, to instigate an arrhythmia due to the irritability of the injured myocardium. I believe this is a likely relationship although once again let me remind you of the appreciable number of patients who spontaneously, without digitalis administration, develop rhythmic disturbances including ventricular tachycardia and ventricular fibrillation. Therefore, I again repeat that if the drug is indicated it should be administered but with caution and careful supervision.

Embolism. This occurs in 12 per cent of cases of myocardial infarction.[2] It usually takes place during the first six or eight weeks. The source of the emboli is usually the mural thrombus in the left ventricle which commonly forms on the endocardial surface of the infarct. Some day it may be demonstrated that this will be prevented by the use of an anticoagulant such as heparin or dicoumarin. Emboli may lodge in any part of the systemic or pulmonary circulation, depending on the site of origin, but the brain, the peripheral arteries of the extremities, and the lungs are the most important sites. Pulmonary emboli are apt to occur later, after the third week, since their source is usually not in the heart but in the veins of the pelvis or lower extremities. Here throm-

bus formation is initiated by the prolonged inactivity of the patient and other concomitant factors. Large emboli breaking off from these sites are occasionally the cause of sudden death during the course of myocardial infarction.

The treatment of choice includes immediate intravenous papaverine in large doses, 0.1 to 0.2 gm. (1½ to 3 gr.), repeated in two hours if needed.[49,50,51] This drug may bring about a rapid return of color and function to the affected extremity accompanied by disappearance of pain. It may also be useful in cerebral embolism and very definitely so for pulmonary emboli. When the extremities are involved, paravertebral sympathetic block is another beneficial measure in some cases in reducing vasconstriction of collateral vessels as well as in major vessels. Embolectomy is probably too dangerous in the presence of fresh myocardial infarction because of the bad operative risk in these patients. However, Pratt[52] believes that embolectomy is indicated in every instance when the diagnosis is made, even though an occasional patient will survive without the removal of the embolus.

Diabetes Mellitus. That coronary occlusion with myocardial infarction is not an infrequent occurrence in the patient with diabetes mellitus is common knowledge. It also is generally known that caution must be exercised in the use of insulin in this combination of diseases. Although glycosuria and hyperglycemia may be treated conservatively in such instances, acidosis cannot, since it may cause death. Nevertheless, some[53] feel that insulin should not be used in the presence of coronary thrombosis since it is said to place an added burden upon the heart and may cause hypoglycemic shock, acute coronary insufficiency, or even death. Having seen several patients with myocardial infarction needlessly go into diabetic coma because insulin was withheld, I am rather adamant in stating that this drug should not be withheld, if needed, even when diabetes is complicated by coronary occlusion. Obviously both the dietary regime and insulin administration in these patients should be modified. This may be done by reducing each individual dose but, if necessary, increasing the number of injections so as to avoid hypoglycemia and yet be sufficient to prevent acidosis.

In some unpublished experiments performed by Ralli,[54] diabetic patients in the arteriosclerotic age period, including some with a diagnosis of coronary sclerosis, were given insulin in divided doses sufficient to prevent hyperglycemia and glycosuria but not enough to cause hypo-

glycemia. Serial electrocardiograms were taken frequently during the course of administration. In none were there any obvious deviations from the normal.

As Joslin[55] has recently emphasized "diabetic coma is an acute deficiency state, a condition in which the primary disturbance is a lack of insulin." He also states that "when a patient with diabetes is seen in diabetic coma it is proof that someone has blundered and, if death due to diabetic coma occurs, the rule still holds." I should like to add that this holds true even when the patient has a complicating coronary occlusion.

It apparently is wiser to use regular insulin in patients with myocardial infarction since severe insulin shock seems more apt to occur with protamine zinc insulin.[56]

In closing I merely wish to say that I have only touched on what I felt were the highlights of the problem assigned to me for discussion.

REFERENCES

1. *New York Times,* Aug. 24, 1942.
2. de la Chapelle, C. E. *Unpublished data.*
3. Prandoni, A. and Wright, I. The anticoagulants, *Bull. New York Acad. Med.,* 1942, *18:*433.
4. Solandt, D. Y. and Best, C. H. Heparin and coronary thrombosis in experimental animals, *Lancet,* 1938, *2:*130.
5. Best, C. H. Heparin and thrombosis, *Bull. New York Acad. Med.,* 1941, *17:* 796.
6. Duryee, W. *Personal communication.*
7. Best, C. H. *Personal communication.*
8. Katz, L. N. and Lindner, E. The reaction of the coronary vessels to drugs and other substances, *J.A.M.A.,* 1939, *113:* 2116.
9. Wilson, F. N. and Johnston, F. D. The occurrence in angina pectoris of electrocardiographic changes similar in magnitude and in kind to those produced by myocardial infarction, *Am. Heart J.,* 1941, *22:*64.
10. Graybiel, A. and Glendy, R. E. Circulatory effects following the intravenous administration of pitressin in normal persons and in patients with hypertension and angina pectoris, *Am. Heart J.,* 1941, *21:*481.
11. Goodman, L. S. Some recent advances in drug therapy, *Bull. New York Acad. Med.,* 1942, *18:*112.
12. Batterman, R. C. *Personal communication.*
13. LeRoy, G. V., Fenn, G. K. and Gilbert, N. C. The influence of xanthine drugs and atropine on the mortality rate after experimental occlusion of a coronary artery, *Am. Heart J.,* 1942, *23:*637.
14. McEachern, C. G., Manning, G. W. and Hall, G. E. Effect of sudden occlusion of coronary arteries following removal of the cardiosensory pathways, *Arch. Int. Med.,* 1940, *65:*661.
15. Manning, G. W., McEachern, C. G. and Hall, G. E. Reflex coronary artery spasm following sudden occlusion of other coronary branches, *Arch. Int. Med.,* 1939, *64:*661.
16. Gilbert, N. C. Influence of extrinsic factors on the coronary flow and clinical course of heart disease, *Bull. New York Acad. Med.,* 1942, *18:*83.
17. Smith, F. M., Rathe, H. W. and Paul, W.D. Theophylline in the treatment of diseases of the coronary arteries, *Arch. Int. Med.,* 1935, *56:*1250.
18. McMahon, A. and Nussbaum, R. A. The

use and abuse of theophylline and its derivatives, *South. M. J.*, 1940, *33:*1127.

19. McMahon, A. and Nussbaum, R. A. Aminophylline, its uses and its effect on the electrocardiogram, *J. Oklahoma M. A.*, 1940, *33:*1.
20. Fowler, W. M., Hurewitz, H. M. and Smith, F. M. The effect of theophylline ethylendiamin on experimentally induced cardiac infarction in the dog, *Am. Heart J.*, 1934-35, *10:*395.
21. Wiggers, C. J. and Green, H. D. The ineffectiveness of drugs upon collateral flow after experimental coronary occlusion in dogs, *Am. Heart J.*, 1936, *11:* 527.
22. Gold, H., Travell, J. and Modell, W. The effect of theophylline with ethylendiamine (aminophylline) on the course of cardiac infarction following experimental coronary occlusion, *Am. Heart J.*, 1937, *14:*284.
23. Levy, R. L., Bruenn, H. G. and Williams, M. E. The modifying action of certain drugs (aminophylline, nitrites, digitalis) upon the effects of induced anoxemia in patients with coronary insufficiency, *Am. Heart J.*, 1940, *19:*639.
24. Gold, H., Kwit, N. T. and Otto, H. The xanthines in the treatment of cardiac pain, *J.A.M.A.*, 1937, *108:*2173.
25. Master, A. M., Jaffe, H. L. and Dack, S. The drug treatment of angina pectoris due to coronary artery disease, *Am. J. M. Sc.*, 1939, *197:*774.
26. Riseman, J. E. F. and Brown, M. G. Medicinal treatment of angina pectoris, *Arch. Int. Med.*, 1937, *60:*100.
27. LeRoy, G. V. The effectiveness of the xanthine drugs in the treatment of angina pectoris, *J.A.M.A.*, 1941, *116:*921.
28. Nichol, E. S. *Personal communication.*
29. Lindner, E. and Katz, L. N. Further observations on the action of drugs on the caliber of coronary vessels. Papaverine hydrochloride, digitalis derivatives, aminophylline, caffeine, glucose, calcium gluconate and metrazol, *J. Pharmacol. & Exper. Therap.*, 1941, *72:*306.
30. McEachern, C. G., Smith, F. H. and Manning, G. W. The effect of intravenous injection of papaverine hydrochloride upon the mortality resulting from sudden occlusion of coronary arteries in dogs, *Am. Heart J.*, 1941, *21:*25.
31. Lindner, E. and Katz, L. N. Papaverine hydrochloride and ventricular fibrillation, *Am. J. Physiol.*, 1941, *133:*155.
32. Elek, S. R. and Katz, L. N. Some clinical uses of papaverine in heart disease, *J.A.M.A.*, 1942, *120:*434.
33. Barach, A. L. and Levy, R. L. Oxygen in the treatment of acute coronary occlusion, *J.A.M.A.*, 1934, *103:*1690.
34. Levy, R. L., ed. *Diseases of the coronary arteries and cardiac pain.* New York, Macmillan Co., 1936, p. 349.
35. Barach, A. L. Recent advances in inhalation therapy in the treatment of cardiac and respiratory disease; principles and methods, *New York State J. Med.*, 1937, *37:*1095.
36. Barach, A. L., Martin, J. and Eckman, M. Positive pressure respiration and its application to the treatment of acute pulmonary edema, *Ann. Int. Med.*, 1938-39, *12:*754.
37. Fishberg, A. M. *Heart failure.* Philadelphia, Lea & Febiger, 1937, p. 617.
38. Warfield, L. M. The treatment of circulatory failure, *J.A.M.A.*, 1936, *106:* 892.
39. Fromet, R. *Les tachycardies paroxystiques ventriculaires.* Paris, Masson, 1932; abstr. *Am. Heart J.*, 1932-33, *8:*294.
40. Stempien, S. J. and Katz, K. H. Quinidine and potassium in the treatment of refractory paroxysmal ventricular tachycardia, *Am. Heart J.*, 1942, *24:*555.
41. Sampson, J. J. and Anderson, E. M. The treatment of certain cardiac arrhythmias with potassium salts, *J.A.M.A.*, 1932, *99:*2257.
42. Smith, H. L. and Boland, E. W. The treatment of auricular fibrillation with quinidine and strychnine, *J.A.M.A.*, 1939, *113:*1017.
43. Kountz, W. B., Smith, J. R. and Wright, S. T. Observations on the effect of tourniquets on acute cardiac crises, normal subjects, and chronic heart failure, *Am. Heart J.*, 1942, *23:*624.
44. Barker, M. H., Lindberg, H. A. and Thomas, M. E. Sudden death and mer-

curial diuretics, *J.A.M.A.*, 1942, *119:* 1001.

45. Brown, G., Friedfeld, L., Kissin, M., Modell, W. and Sussman, R. M. Deaths immediately following the intravenous administration of mercupurin, *J.A.M.A.*, 1942, *119:*1004.
46. DeGraff, A. C. and Nadler, J. E. A review of the toxic manifestations of mercurial diuretics in man, *J.A.M.A.*, 1942, *119:*1006.
47. Editorial. Toxicity of mercurial diuretics, *J.A.M.A.*, 1942, *119:*1026.
48. de la Chapelle, C. E. Spontaneous rupture of the heart, *Am. Heart J.*, 1925-26, *1:*315.
49. Allen, E. V. and MacLean, A. R. Treatment of sudden arterial occlusion with papaverine hydrochloride, *Proc. Staff Meet., Mayo Clin.*, 1935, *10:*216.
50. de Takáts, G. The use of papaverine in acute arterial occlusion, *J.A.M.A.*, 1936, *106:*1003.
51. Atlas, L. N. Management of acute embolic occlusion of arteries to extremities, *Surg., Gynec. & Obst.*, 1942, *74:*236.
52. Pratt, G. H. Surgical treatment of peripheral embolism and aneurysm, *Bull. New York Acad .Med.*, 1942, *18:*586.
53. Levy, R. L. and Bruenn, H. G. Acute, fatal coronary insufficiency, *J.A.M.A.*, 1936, *106:*1080.
54. Ralli, E. P. *Personal communication.*
55. Joslin, E. P., Root, H. F., White, P. and Marble, A. Diabetic coma, *J.A.M.A.*, 1942, *119:*1160.
56. Ralli, E. P., Brandaleone, H. and Fein, H. D. Observations on comparable effects of protamine zinc and regular insulin in diabetic patients followed over a period of years, *Ann. Int. Med.*, 1942, *16:*750.